

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (original) A pharmaceutical dosage form which comprises (a) a first drug which comprises at least one morphine derivative having antitussive activity and (b) at least one second drug, wherein the dosage form provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70 % of a period over which the dosage form provides a plasma concentration within a therapeutic range of the first drug.
2. (original) The dosage form of claim 1, wherein the at least one of morphine derivative comprises at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.
3. (original) The dosage form of claim 2, wherein the first drug comprises at least one of codeine phosphate, dihydrocodeine bitartrate and hydrocodone bitartrate.
4. (original) The dosage form of claim 2, wherein the first drug comprises codeine phosphate.
5. (original) The dosage form of claim 2, wherein the at least one second drug comprises at least one of a decongestant, expectorant, mucus thinning drug, and antihistamine.

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6. (original) The dosage form of claim 1, wherein the at least one second drug comprises a decongestant.

7. (original) The dosage form of claim 6, wherein the second drug comprises at least one of phenylephrine, pseudoephedrine and pharmaceutically acceptable salts thereof.

8. (original) The dosage form of claim 2, wherein the at least one second drug comprises an antihistamine.

9. (original) The dosage form of claim 8, wherein the antihistamine comprises at least one of chlorpheniramine, promethazine, carbinoxamine and pharmaceutically acceptable salts thereof.

10. (original) The dosage form of claim 1, wherein the at least one second drug comprises an expectorant.

11. (original) The dosage form of claim 10, wherein the expectorant comprises guaifenesin.

12. (original) The dosage form of claim 5, wherein a plasma half-life of the at least one second drug differs from a plasma half-life of the first drug by at least about 2 hours.

13. (original) The dosage form of claim 3, wherein a plasma half-life of the at least one second drug

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differs from a plasma half-life of the first drug by at least about 3 hours.

14. (original) The dosage form of claim 1, wherein a plasma half-life of the at least one second drug differs from a plasma half-life of the first drug by at least about 4 hours.

15. (original) The dosage form of claim 5, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 80 % of the period of a plasma concentration within the therapeutic range of the first drug.

16. (original) The dosage form of claim 2, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 90 % of the period of a plasma concentration within the therapeutic range of the first drug.

17. (original) The dosage form of claim 1, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 95 % of the period of a plasma concentration within the therapeutic range of the first drug.

18. (original) The dosage form of claim 1, wherein the dosage form comprises a tablet.

19. (original) The dosage form of claim 18, wherein the tablet comprises at least two layers.

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20. (original) The dosage form of claim 19, wherein the tablet is a bi-layered tablet.

21. (original) The dosage form of claim 18, wherein the tablet comprises a matrix which comprises the first drug and has dispersed therein particles which comprise the at least one second drug.

22. (cancelled)

23. (original) A bi-layered tablet which comprises a first layer and a second layer, the first layer comprising a first drug which comprises at least one morphine derivative having antitussive activity, and the second layer comprising at least one second drug which is selected from decongestants, expectorants, mucus thinning drugs, and antihistamines, wherein the bi-layered tablet provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70 % of a period over which the bi-layered tablet provides a plasma concentration within a therapeutic range of the first drug.

24. (original) The bi-layered tablet of claim 23, wherein the first layer comprises at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

25. (original) The bi-layered tablet of claim 24, wherein the second layer comprises at least one of phenylephrine, pseudoephedrine, chlorpheniramine, carbinoxamine, promethazine, guaifenesin and pharmaceutically acceptable salts thereof.

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26. (original) The bi-layered tablet of claim 24, wherein the tablet comprises at least two of phenylephrine, pseudoephedrine, chlorpheniramine, carbinoxamine, promethazine, guaifenesin and pharmaceutically acceptable salts thereof.

27. (original) The bi-layered tablet of claim 23, wherein the first layer only comprises one or more of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof as active ingredient(s).

28. (original) The bi-layered tablet of claim 24, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 80 % of the period of a plasma concentration within the therapeutic range of the first drug.

29. (original) The bi-layered tablet of claim 25, wherein the period of a plasma concentration within a therapeutic range of the at least one second drug is coextensive with at least about 90 % of the period of a plasma concentration within a therapeutic range of the first drug.

30. (original) The bi-layered tablet of claim 23, wherein at least one of the first and second layers is an immediate release layer.

31. (original) The bi-layered tablet of claim 30, wherein the first layer is an immediate release layer.

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32. (original) The bi-layered tablet of claim 30, wherein the second layer is an immediate release layer.

33. (original) The bi-layered tablet of claim 23, wherein both of the first and second layers are controlled release layers.

34. (original) The bi-layered tablet of claim 24, wherein the first layer comprises a total of from about 0.1 mg to about 120 mg of at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

35. (original) The bi-layered tablet of claim 34, wherein the first layer comprises a total of from about 5 mg to about 90 mg of at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

36. (original) The bi-layered tablet of claim 35, wherein the first layer comprises a total of from about 25 mg to about 50 mg of at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

37. (original) The bi-layered tablet of claim 34, wherein the second layer comprises at least one of (i) from about 0.1 mg to about 16 mg of chlorpheniramine maleate or an equivalent amount of at least one other pharmaceutically acceptable salt of chlorpheniramine; (ii) from about 1 mg to about

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90 mg of phenylephrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of phenylephrine; (iii) from about 1 mg to about 240 mg of pseudoephedrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of pseudoephedrine; (iv) from about 0.1 mg to about 75 mg of promethazine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of promethazine; (v) from about 0.1 mg to about 32 mg of carbinoxamine maleate or an equivalent amount of at least one other pharmaceutically acceptable salt of carbinoxamine; and (vi) from about 1 mg to about 2400 mg of guaifenesin or an equivalent amount of at least one pharmaceutically acceptable salt of guaifenesin.

38. (original) The bi-layered tablet of claim 35, wherein the first layer comprises at least one of (i) from about 1 mg to about 90 mg of phenylephrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of phenylephrine; and (ii) from about 1 mg to about 240 mg of pseudoephedrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of pseudoephedrine, and the second layer comprises at least one of an antihistamine and an expectorant.

39. (original) A multi-layered tablet which comprises at least a first layer and a second layer, wherein the first layer comprises at least one of codeine, dihydrocodeine, hydrocodone and a pharmaceutically acceptable salt thereof and the second layer comprises at least one drug which is selected from decongestants, expectorants, mucus thinning drugs, analgesics and antihistamines.

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40. (original) The multi-layered tablet of claim 39, wherein the first layer is an immediate release layer.

41. (original) The multi-layered tablet of claim 39, wherein the first layer is a controlled release layer.

42. (original) The multi-layered tablet of claim 41, wherein the second layer is a controlled release layer.

43. (original) The multi-layered tablet of claim 39, wherein the first layer comprises at least one of codeine phosphate, dihydrocodeine bitartrate and hydrocodone bitartrate.

44. (original) The multi-layered tablet of claim 42, wherein the first layer does not contain any active ingredient which is different from codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

45. (original) The multi-layered tablet of claim 39, wherein the tablet comprises at least one of dextromethorphan, phenylephrine, pseudoephedrine, guaifenesin, chlorpheniramine, carbinoxamine, promethazine and pharmaceutically acceptable salts thereof.

46. (original) The multi-layered tablet of claim 39, wherein the tablet comprises at least two of

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dextromethorphan, phenylephrine, pseudoephedrine, guaifenesin, chlorpheniramine, carbinoxamine, promethazine and pharmaceutically acceptable salts thereof.

47. (currently amended) The multi-layered tablet of claim 39, wherein the at least one drug in the second layer has a plasma half-life which differs by at least about 1 hour from ~~the~~ a plasma half-life of the at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

48. (original) The multi-layered tablet of claim 47, wherein the tablet provides a plasma concentration within a therapeutic range of the at least one drug in the second layer over a period which is coextensive with at least about 80 % of a period over which the tablet provides a plasma concentration within a therapeutic range of the at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

49. (original) The multi-layered tablet of claim 48, wherein the at least one drug in the second layer comprises one or more of phenylephrine, pseudoephedrine, chlorpheniramine and pharmaceutically acceptable salts thereof.

50. (original) The multi-layered tablet of claim 39, wherein the layers are discrete zones which are arranged adjacent to each other.

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51. (original) The multi-layered tablet of claim 39, wherein the second layer is partially or completely surrounded by the first layer.

52. (original) The multi-layered tablet of claim 39, wherein the second layer is coated with the first layer.

53. – 63. (cancelled)

64. (withdrawn) A method of concurrently alleviating a condition which can be alleviated by administering codeine, dihydrocodeine, or hydrocodone and at least one other condition which can be alleviated by administering a drug which is at least one of a decongestant, expectorant, mucus thinning drug, and antihistamine, wherein the method comprises administering the pharmaceutical dosage form of claim 1 to a subject in need thereof.

65. (withdrawn) A method of concurrently alleviating a condition which can be alleviated by administering codeine, dihydrocodeine, or hydrocodone and at least one other condition which can be alleviated by administering a drug which is at least one of a decongestant, expectorant, mucus thinning drug, and antihistamine, wherein the method comprises administering the multi-layered tablet of claim 39 to a subject in need thereof.

66. (withdrawn) The method of claim 65, wherein the condition which can be alleviated by

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administering codeine, dihydrocodeine, or hydrocodone comprises coughing.

67. (withdrawn) The method of claim 64, wherein the dosage form is administered not more than about three times per day.

68. (withdrawn) The method of claim 67, wherein the multi-layered tablet is administered not more than about twice per day.

69. (cancelled)

70. (withdrawn) A process of making the pharmaceutical dosage form of claim 1, wherein the method comprises preparing a first composition which comprises the first drug and a second composition which comprises the at least one second drug, and combining the first and the second compositions to form the dosage form.

71. (withdrawn) The process of claim 70, wherein the first and second compositions are combined by using a tablet press.

72. (original) A pharmaceutical dosage form which comprises (a) a first drug which comprises at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof and has a first plasma half-life and (b) at least one second drug which is selected from decongestants,

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expectorants, mucus thinning drugs, and antihistamines and has a second plasma half-life which differs from the first plasma half-life by at least about 2 hours, wherein the dosage form provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 80 % of a period over which the dosage form provides a plasma concentration within a therapeutic range of the first drug.

73. (original) The dosage form of claim 72, wherein the first plasma half-life differs by at least about 3 hours from the second plasma half-life.

74. (original) The dosage form of claim 72, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 90 % of the period over which the dosage form provides a plasma concentration within the therapeutic range of the first drug.

75. (original) The dosage form of claim 74, wherein the dosage form comprises a multi-layered tablet.

76. (original) The dosage form of claim 72, wherein the dosage form is associated with instructions to administer the dosage form three or fewer times per day.

77. (original) The dosage form of claim 75, wherein the dosage form is associated with instructions

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to administer the dosage form once or twice per day.

78. (currently amended) A pharmaceutical dosage form which comprises (a) at least one first morphine derivative in a first form or layer and (b) at least one second morphine derivative which is different from the first morphine derivative in a second form or layer which is different from the first form or layer, wherein the dosage form releases the at least one first morphine derivative at least one of over a different period and at a different rate than the at least one second morphine derivative.

79. (cancelled)

80. (original) The dosage form of claim 78, wherein the at least one first morphine derivative and the at least one second morphine derivative are independently selected from codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

81. (currently amended) The dosage form of claim [[79]] 80, wherein the at least one first morphine derivative and the at least one second morphine derivative comprise at least one of codeine phosphate, dihydrocodeine bitartrate and hydrocodone bitartrate.

82. (original) The dosage form of claim 78, wherein the dosage form comprises codeine phosphate.

83. (original) The dosage form of claim 80, wherein the first form or layer is an immediate release

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form or layer and the second form or layer is a controlled release form or layer.

84. (original) The dosage form of claim 78, wherein the dosage form is a multi-layered tablet which comprises at least one immediate release layer and at least one controlled release layer which independently comprise at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

85. (original) The dosage form of claim 84, wherein the dosage form further comprises at least one additional drug which is selected from decongestants, expectorants, mucus thinning drugs, and antihistamines.

86. (original) The dosage form of claim 85, wherein at least the immediate release layer thereof comprises the at least one additional drug.

87. (original) The dosage form of claim 85, wherein at least the controlled release layer thereof comprises the at least one additional drug.

88. – 91. (cancelled)

92. (original) The dosage form of claim 78, wherein the dosage form releases the at least one first morphine derivative over a different period and at a different rate than the at least one second

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morphine derivative.

93. (original) The dosage form of claim 78, wherein the dosage form releases the at least one first morphine derivative over a different period than the at least second morphine derivative.

94. (original) The dosage form of claim 93, wherein the dosage form releases the at least one first morphine derivative over a first period and the at least one second morphine derivative over a second period and not more than about 30 % of the second period are coextensive with all or a part of the first period.

95. (original) The dosage form of claim 94, wherein there is substantially no overlap between the first and second periods.

96. (original) The dosage form of claim 78, wherein the dosage form releases the at least one first morphine derivative at a different rate than the at least second morphine derivative.

97. (cancelled)

98. (cancelled)

99. (new) A bi-layered tablet which comprises a first layer and a second layer, the first layer

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comprising a first drug which is selected from codeine and pharmaceutically acceptable salts thereof, and the second layer comprising at least one second drug which is selected from decongestants, expectorants, mucus thinning drugs, and antihistamines, wherein the bi-layered tablet provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70 % of a period over which the bi-layered tablet provides a plasma concentration within a therapeutic range of the first drug.

100. (new) The bi-layered tablet of claim 99, wherein the first layer comprises codeine phosphate.

101. (new) The bi-layered tablet of claim 100, wherein the second layer comprises at least one of phenylephrine, pseudoephedrine, chlorpheniramine, carbinoxamine, promethazine, guaifenesin and pharmaceutically acceptable salts thereof.

102. (new) The bi-layered tablet of claim 100, wherein the tablet comprises at least two of phenylephrine, pseudoephedrine, chlorpheniramine, carbinoxamine, promethazine, guaifenesin and pharmaceutically acceptable salts thereof.

103. (new) The bi-layered tablet of claim 99, wherein the first layer comprises only one or more of codeine and pharmaceutically acceptable salts thereof as active ingredient(s).

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104. (new) The bi-layered tablet of claim 99, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 80 % of the period of a plasma concentration within the therapeutic range of the first drug.

105. (new) The bi-layered tablet of claim 100, wherein the period of a plasma concentration within a therapeutic range of the at least one second drug is coextensive with at least about 90 % of the period of a plasma concentration within a therapeutic range of the first drug.

106. (new) The bi-layered tablet of claim 99, wherein at least one of the first and second layers is an immediate release layer.

107. (new) The bi-layered tablet of claim 106, wherein the first layer is an immediate release layer.

108. (new) The bi-layered tablet of claim 106, wherein the second layer is an immediate release layer.

109. (new) The bi-layered tablet of claim 99, wherein both of the first and second layers are controlled release layers.

110. (new) The bi-layered tablet of claim 99, wherein the first layer comprises a total of from

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about 5 mg to about 90 mg of at least one of codeine and a pharmaceutically acceptable salt thereof.

111. (new) The bi-layered tablet of claim 99, wherein the first layer comprises a total of from about 25 mg to about 50 mg of at least one of codeine phosphate.

112. (new) The bi-layered tablet of claim 110, wherein the second layer comprises at least one of (i) from about 0.1 mg to about 16 mg of chlorpheniramine maleate or an equivalent amount of at least one other pharmaceutically acceptable salt of chlorpheniramine; (ii) from about 1 mg to about 90 mg of phenylephrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of phenylephrine; (iii) from about 1 mg to about 240 mg of pseudoephedrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of pseudoephedrine; (iv) from about 0.1 mg to about 75 mg of promethazine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of promethazine; (v) from about 0.1 mg to about 32 mg of carbinoxamine maleate or an equivalent amount of at least one other pharmaceutically acceptable salt of carbinoxamine; and (vi) from about 1 mg to about 2400 mg of guaifenesin or an equivalent amount of at least one pharmaceutically acceptable salt of guaifenesin.

113. (new) The bi-layered tablet of claim 111, wherein the first layer comprises at least one of (i) from about 1 mg to about 90 mg of phenylephrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of phenylephrine; and (ii) from about 1 mg to about 240

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mg of pseudoephedrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of pseudoephedrine, and the second layer comprises at least one of an antihistamine and an expectorant.

114. (new) The dosage form of claim 4, wherein the second drug comprises at least one drug selected from phenylephrine, pseudoephedrine and pharmaceutically acceptable salts thereof.

115. (new) The dosage form of claim 4, wherein the at least one second drug comprises at least one drug selected from chlorpheniramine, promethazine, carbinoxamine and pharmaceutically acceptable salts thereof.

116. (new) The dosage form of claim 4, wherein the at least one second drug comprises guaifenesin.